## **ABSTRACT**

The invention includes compositions and methods for the selective inhibition of cytokine-mediated NF- $\kappa$ B activation by blocking the interaction of NEMO with I $\kappa$ B kinase- $\beta$  (IKK $\beta$ ) at the NEMO binding domain (NBD). The blockade of IKK $\beta$ -NEMO interaction resulting in inhibition of IKK $\beta$  kinase activity and subsequent decreased phosphorylation of I $\kappa$ B. Phosphorylation of I $\kappa$ B being an integral step in cytokine-mediated NF- $\kappa$ B activation. The invention further includes methods for screening for agents capable of interacting at the NBD and therapeutic uses for such agents in pathological disorders caused by dysregulation of NF- $\kappa$ B activation.

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